REMARKS

Claims 27, 28, 32, 33, 38, 39, 43, 44, and 49-64 are pending in this application. Claims 29-31, 34-37, 40-42, and 45-48, drawn to a nonelected invention, have been canceled without prejudice or disclaimer. Claims 49-64 have been added and depend directly or indirectly from claims 27, 28, 38, and 39 and further describe the viral genome as one of HIV-1 Bru, HIV-1 Mal, HIV-1 Eli, HIV-2 ROD, or SIV-1 MAC. Support for these new claims can be found throughout the specification, including, for example, at page 4. This Amendment does not introduce new matter into the specification.

Abstract

The Examiner noted that this application does not contain an abstract of the disclosure. (Paper No. 15, p. 3.) Applicants submit with this response an abstract of the disclosure on a separate sheet as required by 37 C.F.R. § 1.72(b).

Rejections Under 35 U.S.C. § 112, First Paragraph

1. Written Description

The Office rejected claims 27, 28, 32, 33, 38, 39, 43 and 44 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art, at the time the application was filed, that the inventors had possession of the claimed invention. (Paper No. 15, p. 3.) Applicants respectfully traverse this rejection.

Applicants identified certain nucleotide sequences that are conserved between different HIV and SIV strains. These sequences are insensitive to much, if any,

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variations in the genomes of different HIV and SIV isolates and, therefore, can be used as primers to amplify nucleotide sequences from different HIV-1, HIV-2, and SIV strains. In claims 27, 28, 38, and 39, the claimed polypeptides are expressed by a method comprising a) using the primers to amplify a nucleic acid encoding the polypeptide, b) introducing the amplified nucleic acid into a vector, c) transforming a host cell with the vector, d) placing the transformed cell in culture, and e) recovering the expressed polypeptide.

Claims 27, 28, 38, and 39 are product-by-process claims,[1] where the claims recite the process by which the product is made. *See* M.P.E.P. § 2173.05(p). Therefore, as an initial matter, this case is not analogous to *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), as asserted by the Office. (Paper No. 15, p. 6.) In *Lilly*, the claims recited vertebrate or mammalian cDNA encoding insulin. They were not product-by-process claims. Instead, the claimed cDNA was defined only by its **function**. *Id.* at 1563. The Federal Circuit affirmed the district court's finding that the description of the rat insulin cDNA did not provide adequate written desciption support for the broad classes of vertebrate or mammalian insulin cDNA. Thus, *Lilly* held that "a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." *Id.* at 1568.

Here, however, unlike *Lilly*, the product claims are not defined by function. Rather, the claimed products are described, in part, by their method of production.

[1] The remaining claims under rejection depend directly from these claims.

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Even the M.P.E.P. recognizes a distinction between the written description support necessary for product claims versus product-by-process claims. For example, the M.P.E.P. states that

> disclosure of only a method of making the invention and the function may not be sufficient to support a product claim **other than a product-by-process claim**. *See, e.g., Fiers v. Revel*, 984 F.2d at 1169, 25 USPQ2d at 1605; *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021. Where the process has actually been used to produce the product, the written description requirement for a product-by-process claim is clearly satisfied; however, the requirement may not be satisfied where it is not clear that the acts set forth in the specfication can be performed, or that the product is produced by the process.

M.P.E.P. § 2163, pp. 2100-163 - 2100-164 (emphasis added).

This distinction is also recognized in the PTO's Synopsis of Application of Written Description Guidelines.[2] In particular, Example 10 analyzes written description support for two claims. Exhibit 1, p. 38. Claim 1 is directed to a process for producing an isolated polynucleotide by hybridizing a specific sequence to genomic DNA under stringent hybridizing conditions. Claim 2 is directed to an isolated DNA that hybridizes with the specific sequence. Under the facts presented in this example, the PTO concluded that the specification provided adequate written description support for the process claim but not the product (i.e., isolated DNA) claim. *Id.* at 40. The Guidelines note, however, that the specification would provide written description support if the product claim were substituted with a product-by-process claim, i.e., the isolated DNA prepared according to the process of claim 1. *Id.* Thus, the PTO recognizes a distinction between the written description support required for product claims versus

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2 Exhibit 1.

product-by-process claims. It does not appear, however, that the Office acknowledged this distinction in the rejection based on the written description requirement.

The Office notes that "there [is not] any indication that the artisan actually implemented the method of the claims to identify such polypeptides." (Paper No. 15, p. 6.) Although an actual reduction to practice is one way to provide written description support, it is not the only way. "It is true that reduction to practice ordinarily provides the best evidence that an invention is complete. But just because reduction to practice is sufficient evidence of completion, it does not follow that proof of reduction to practice is necessary in every case." *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 66 (1998).[3]

As noted above, the M.P.E.P. states that for a product-by-process claims, like the claims at issue here, "the [written description] requirement may not be satisfied where it is not clear that the acts set forth in the specfication can be performed, or that the product is produced by the process." M.P.E.P. § 2163, pp. 2100-163 - 2100-164. Conversely, therefore, if the process steps recited in the claim can be performed and if the claimed product is produced, the written description requirement should be satisfied. That is precisely the case here.

The specification discloses the amplification of numerous nucleic acids using the primers recited in the claims. (Specification, pages 15-18.) Tables II, III, and IV on pages 18-20 discloses 27 different nucleic acid sequences that were amplified from the *env* gene using different sets of primers and different HIV strains. The specification also teaches that such amplified sequences can be translated into polypeptides. (*See*,

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3 *See also*, M.P.E.P. § 2163, pp. 2100-160 - 2100-161 (citing *Pfaff* for this proposition).

Specification, pp. 25-26.) For example, the amplified sequences can be introduced into a vector, which can be used to transform a cell, where the amplified sequence can be translated into a polypeptide and recovered. Although the specification does not disclose an actual working example where these amplified nucleic acid sequences were translated into a polypeptide, such methods of expressing recombinant DNA in host cells were well known in the art at the time of the invention. For example, the Second Edition (1989) of Molecular Cloning: A Laboratory Manual, discusses in depth the expression of recombinant nucleotide sequences in various host cells.[4] Information that is well known in the art need not be described in detail in the specification. M.P.E.P. § 2163, p. 2100-160 (citing *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80 (Fed. Cir. 1986).

Furthermore, the Office bears the burden of presenting by preponderance of the evidence why one of skill in the art would not recognize in applicants' disclosure a description of the claimed invention. Thus, in this case, with product-by-process claims, the Office must provide sufficient evidence or reasoning explaining why the recited process cannot be performed, or why the claimed product is not produced by the recited process. *See*, M.P.E.P. § 2163, pp. 2100-163 - 2100-164; *see also*, M.P.E.P. § 2163.04. The Office has not provided this evidence or reasoning. Therefore, the description as filed is presumed adequate. *See*, M.P.E.P. § 2163.04.

Given the level of skill and knowledge in the art of recombinant DNA technology, there is no reason to doubt that one of skill in the art at the time of the invention could

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4 J. Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, 16.1-17.44 (2nd Ed. 1989)(Exhibit 2).

have taken viral nucleotide sequences, such as the amplified viral sequences disclosed in the specification and, using well-known molecular biology techniques, expressed the polypeptides encoded by those nucleotide sequences, as recited in the claims. Indeed, even the Examiner appears to acknowledge that one of skill in the art, relying on common, general knowledge would understand how to use the claimed process steps to obtain the claimed polypeptides. Specifically, the Office states:

> Although the description does not provide working examples of the compounds, the description teaches a method for applying PCR to discover nucleotide sequences which encode undisclosed polypeptide fragments and the person skilled in the art can understand how to use the screening method considering the common general knowledge.

(Paper No. 15, p. 4.)[5]

The Examiner's acknowledgement is likewise consistent with the PTO's issuance of U.S. Patent No. 5,786,177 ("the '177 patent"), which is based on the same disclosure as the present application.[6] The claims of the '177 patent are directed to methods of preparing a polypeptide encoded by the HIV or SIV genome comprising a) amplifying a nucleic acid with at least two primers (including the primers recited in the pending claims); b) introducing the amplified nucleotide sequence into a vector; c) transforming a host cell with the vector; and d) placing the transformed host cell in culture and recovering the polypeptide from the culture. The PTO found that these method claims, which recite similar steps as those in the current product-by-process claims, satisfied

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[5] It is not clear what screening method the Office refers to, because the process recited in the claims involves amplifying a viral nucleotide sequence, expressing a polypeptide encoded by the nucleotide sequence, and recovering the polypeptide.

[6] Although the '177 patent has already been cited in an IDS, for the convenience of the Examiner, applicants enclose a copy of the '177 patent as Exhibit 3.

the statutory requirements for patentability, including 35 U.S.C. § 112, first paragraph. Thus, the '177 patent further provides further support that the process steps recited in the pending claims can be performed and will result in the production of the the claimed polypeptide. *See*, M.P.E.P. § 2163, pp. 2100-163 - 2100-164; 2163.04.

Moreover, the Examiner in this application does not appear to dispute that the specification provides written description support for at least some of the polypeptides encompassed by the claims. Specifically, the Office states that applicants were in possession of the claimed sequences drawn to the specific viral strains disclosed in the specification, including HIV-1 Mal, HIV-1-Eli, HIV-1 Bru, HIV-2 Rod, and SIV-1 Mac. (Paper No. 15, p. 3.) However, the Office asserts that "applicants were not in possession of yet undiscovered and mutated new viral strains as encompassed by the instant claims." (*Id.* at 4.) Thus, the Office appears to take the position that the specification does not provide adequate written description support for the full scope of the claims.

Missing from the Office's analysis, however, is any evidence or reasoning explaining why one of skill in the art would understand that applicants were in possession of certain polypeptides but not others, particularly given that these are product-by-process claims. If the specification adequately describes a process for obtaining certain polypeptides and claims the polypeptides as products of that process, then the specification adequately describes the claimed polypeptides. The Office has not presented any reasoning or evidence to suggest that certain polypeptides encompassed by the claims could not be obtained from certain HIV or SIV strains. Thus, the Office provides no basis to distinguish between a claimed polypeptide derived

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from one of the viral strains disclosed in the specification and a claimed polypeptide derived, for example, from a variant strain of one of the viral strains disclosed in the specification.

Finally, the Office asserts that "[t]he claims encompass a genus of compounds defined only by their method of obtaining the compound wherein the relationship between the structural features of members of the genus and said method have not been defined." (Paper No. 15, p. 4.) The Office's characterization, however, is inaccurate. As discussed above, these are product-by-process claims, and, therefore, they are distinguishable from the product claims of *Lilly* that were defined only by their function, i.e., encoding insulin. The process steps recited in the pending claims help to provide relelvant information about the structural features of the claimed polypeptides. Thus, the pending claims provide relevant, identifying characteristics that were absent from the claims at issue in *Lilly*.

As noted in the M.P.E.P.:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), **or by disclosure of relevant, identifying characteristics,** i.e., structures or other physical and/or chemical properties, by functional charactieristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (see i)(C), above).

M.P.E.P. § 2163, p. 2100-164 (emphasis added).

It is inherent in the pending claims that the primers recited in the claims provide guidance regarding the structure and properties of the amplified nucleotides, and

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consequently, the claimed polypeptides.[7] The primers help to define a structural region of the amplified nucleotide sequence that is conserved between different HIV and SIV strains. In addition, because these sequences are conserved among different strains, they possess certain properties that make them useful as primers to amplify nucleotide sequences from different HIV-1, HIV-2, and SIV strains. The resulting polypeptides share in these properties because they are the translated products of the nucleotides amplified using the recited primers. Accordingly, the specification discloses a combination of identifying characteristics regarding the structure and properties of the claimed polypeptides, sufficient to show the applicants were in possession of the claimed genus.

For the reasons discussed above, applicants respectfully request withdrawal of this 35 U.S.C. § 112, first paragraph, written description rejection.

2. Enablement

The Office also rejected claims 27, 28, 32, 33, 38, 39, 43, and 44 under 35 U.S.C. § 112, first paragraph, alleging that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. (Paper No. 15, p. 7.) Applicants respectfully traverse this rejection.

The Office has the initial burden of establishing a *prima facie* case of lack of enablement. (M.P.E.P. § 2164.04.) Applicants' specification disclosing how to make

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[7] Applicants note that the primers can contain some variability in length and nucleotide sequence, as long as the variations do not change the hybridization properties of the primers, i.e., provided the primers maintain their insensitivity to variations in the genomes of different HIV and SIV isolates, as taught in the specification. (Specification, p. 4, lines 6-23; p. 10, lines 27-35; p. 11, lines 1-10.)

and use the claimed invention must be taken as complying with 35 U.S.C. § 112, first paragraph, unless there is reason to doubt the objective truth of the disclosure. *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995). The Office has questioned the enablement provided by applicants' specification but has not given any technical reasons to support the rejection. And although the Office lists the eight *Wands* factors (*see* M.P.E.P. § 2164.01(a)) at page 7 of Paper No. 15, the Office provides no analysis of these factors with respect to the presently pending claims. As stated in *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971)(emphasis in original):

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively correct disclosure.

See also, M.P.E.P. § 2164.04, p. 2100-178.

As discussed above, the specification discloses the amplification of numerous nucleic acids using the primers recited in the claims. (Specification, pages 15-18.) The specification also teaches that such amplified sequences can be translated into polypeptides using, for example, conventional molecular biology and cloning techniques. (*See*, Specification, pp. 25-26.) The Office has not provided any specific technical reasons to doubt the objective truth of these statements.

Furthermore, the PTO's issuance of the '177 patent (discussed above) and U.S. Patent No. 6,194,142 ("the '142 patent"),[8] which like the '177 patent is also based on

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[8] A copy of the '142 patent is attached as Exhibit 4.

the same disclosure as the present application, provides further support that the instant specification enables the full scope of the pending claims. The claims of the '142 patent are similar to the pending claims. Both are product-by-process polypeptide claims. They both recite the process steps of a) amplifying a nucleic acid encoding the polypeptide, b) introducing the amplified nucleic acid into a vector, c) transforming a host cell with the vector, d) placing the transformed cell in culture, and e) recovering the expressed polypeptide. The primers recited in the '142 patent correspond to sequences in genes other than the *env* gene, whereas the primers recited in the pending claims correspond to sequences in the *env* gene. The PTO did not question the enablement of the claims that issued in the '142 patent.

And the Office does not provide any technical reasons for questioning why one of skill in the art could not make the claimed polypeptides using the process steps recited in the pending claims. Rather, the Office states that "the specification does not disclose the structure of the proteins belonging to viral strains and mutants other than those five . . . disclosed in the specification . . . ." (Paper No. 15, p. 8.) The Office further states that "an assay for finding a product is not equivalent to a positive recitation of how to make such a product." (*Id.*) Applicants do not understand this latter statement. Nevertheless, based on these statements, the Office generally concludes that the claims fail to meet the "how to make" prong of the enablment requirement. (*Id.*) As stated above, however, the Office has not provided any evidence or technical reasons to explain why one of skill in the art could not make the claimed polypeptides using the process steps recited in the pending claims. Thus, the Office has not met its initial burden in establishing a *prima facie* case of nonenablement.

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Therefore, if the Office adheres to the rejection based on a non-enabling disclosure, applicants respectfully request that the Office provide reasons one of skill in the art would not be able to make the claimed invention. In the absence of such reasons, applicants respectfully request that the Office reconsider and withdraw this 35 U.S.C. § 112, first paragraph, enablement rejection.

CONCLUSION

In view of the foregoing remarks, applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

If there is any fee due in connection with the filing of this paper, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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